Cartilage Heal Thyself

Tissue-engineered scaffolding may help the body repair weakened knees and joints.

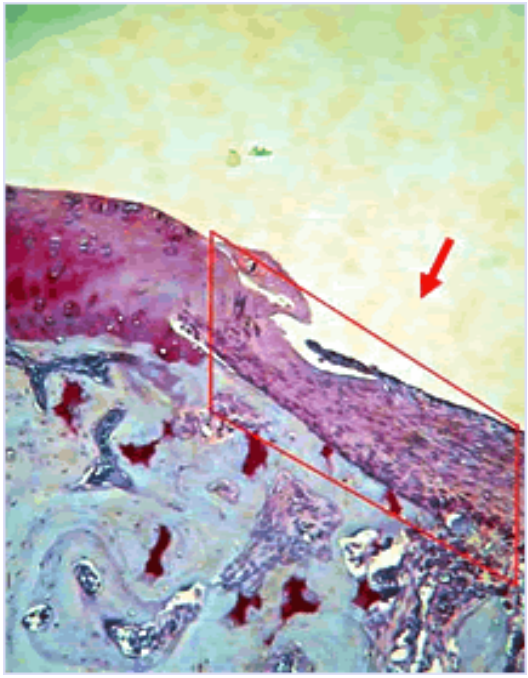
Damaged cartilage in knees and joints, caused by traumatic injury or the regular wear and tear of age, is nearly impossible for the body to repair on its own. Unlike other tissues, cartilage lacks the blood vessels that deliver nutrients and other healing substances to damaged regions. Medical treatment usually aims to alleviate pain and discomfort without mending underlying injuries. Now scientists are working to develop a biomaterial that could help the body use its own resources to replenish damaged cartilage.

Research led by Dr. Lori Setton, associate professor and director of the cartilage mechanics and tissue engineering laboratory at Duke University, has produced a versatile liquid polymer gel that solidifies in 30 seconds when exposed to laser light. This liquid/solid duality allows the material to be injected and "poured" into torn cartilage tissue, where the liquid gel adapts to the contours and size of the cartilage tear. Once in place, the biomaterial is cured to a solid and serves as a scaffold for the body's own chondrocyte cells, which help to rebuild cartilage. The polymer has been used for cartilage repair in vivo in rabbits with promising results.

From Cornea to Cartilage

The idea of this new biomaterial came to Dr. Setton in 1997 after attending an interdisciplinary lecture delivered by Dr. Mark Grinstaff, a chemistry professor at Duke. Dr. Grinstaff initially developed the material from a natural material called hyaluronan, as a liquid for cornea repair. "After the seminar, I asked him if the material could be made stiffer to withstand the mechanical demands of cartilage. We started working together on this and Mark synthesized about five different formulations before we began trying it on animal models," says Dr. Setton.

At the molecular level, the biomaterial behaves like a minute biological scaffold that provides the necessary environment for cartilage cells (chondrocytes) to generate new tissue. Nurturing chondrocyte growth is critical because these cells produce collagen, a thread-like, helical molecule also found in skin and hair, making it the most abundant protein in the body. In a healthy individual, chondrocytes continuously rebuild the collagen in cartilage as it is worn away by the body's normal activities. Without chondrocytes, any implanted biomaterial would not regrow and would eventually fail. The new biomaterial also offers other advantages. "As cells migrate into the biomaterial's scaffold, they grow new cartilage, which eventually replaces the biomaterial," notes Dr. Setton.



In only two weeks, cartilage – one of the most difficult tissues to repair – was regrown in a rabbit knee joint. The newly restored cartilage, stained dark purple on the right, was rebuilt using a new biomaterial that fosters cartilage growth. With further study, this biomaterial may one day help to repair cartilage damage due to injury.
Image courtesy of Dr. Lori Setton, Duke University.

Best of Both Worlds

Currently, physicians treat damaged cartilage with either therapeutic fluid injections or surgery to implant chondrocytes. Injecting the hyaluronan in liquid form directly into joints helps to supplement the joint's own natural lubrication, thereby improving movement and reducing pain for up to six months. The surgical technique involves growing the patient's own cartilage cells in the laboratory and then implanting

them into the tear in the patient's joint. However, the fluid injections require repeated treatments, and the surgical procedure is expensive and necessitates a lingering postsurgical recuperation.

The biomaterial discovered by Dr. Setton and her colleagues offers the best of both worlds by generating pain relief and a long-term solution. "We hope the new procedure will achieve about the same success, or better, than cartilage cell transplantation. And because it is injected and gelled within the defect, it should be better integrated, more durable, and offer a more rapid recovery. The procedure also would be less costly than cell transplantation," she notes.

Partial funding for this research comes from the National Institute of Biomedical Imaging and Bioengineering and from the National Institute of Arthritis and Musculoskeletal and Skin Disorders. Dr. Setton's team is currently expanding its research by working with new versions of natural biomaterials. "We are evaluating these new materials in large animal models, which will hopefully pave the way for a clinical treatment in the future," she says.

Reference

Nettles DL, Vail TP, Morgan MD, Grinstaff MW, Setton LA. Photocrosslinkable hyaluronan as a scaffold for articular cartilage repair. Annals of Biomedical Engineering 32:391-397, 2004.